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Filed: December 22, 2000

### REMARKS

Prior to this amendment, claims labeled as Claims 35-44 were pending. Applicants thank the Examiner for renumbering the claims in compliance with 37 CFR § 1.126. In response, Applicants have amended the claims to reflect the correct numbering of the claims. Following the amendment to correct the claim numbering, claims 40-49 were currently pending. Claim 40 and 42 have been amended. Support for the amendment is found p. 7, lines 5-6, p. 64, lines 21-22, p. 65, lines 7-8 and in the figures, for example figures 8, 9 and 10. Claims 50 and 51 are new. Support for new claim 50 is found in the claims as filed and at p. 34, lines 21-27. Support for new claim 51 is found in the claims as filed and at p. 34, lines 9-10. Applicants submit that no new matter is introduced by way of this amendment. Applicants respectfully request entry of this amendment.

### Priority

The Examiner rejects Applicants' assertion of priority to Provisional Application 60/060,473 and parent application 09/189,543 because, according to the Examiner, the applications do not support the instantly claimed "liquid array". While Applicants disagree with this position, Applicants submit that the rejection is moot as the difference in priority claimed by Applicants and that proposed by the Examiner has no effect on any other rejections because the cited reference does not have an effective filing date between the priority date claimed and that proposed by the Examiner.

### 35 U.S.C. §§ 102(e)

Claims 40-49 stand rejected under 35 U.S.C. § 102 (e) as being anticipated by Kamb *et al.* (U.S. Patent No. 6,060,240). Basically, the Examiner's position appears to

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be that Kamb discloses the elements of the present claims. Applicants respectfully traverse the rejection.

The Examiner cites Kamb as teaching a population of microspheres comprising at least a first and second subpopulation of microspheres comprising at least a first and second decoding attribute and detecting each of the decoding attributes to identify each of the bioactive agents. In actuality, the cited sections teach a competitive binding assay for normalizing libraries or populations of nucleic acids. Specifically, Kamb teaches library cDNAs with identifier tag sequences. Kamb allows these cDNAs to mix in solution with cellular cDNA, labeled with a first label, to form cDNA duplexes of interest. The duplexes are then exposed to capture oligonucleotides (bound to beads) that are complementary to the identifier tag sequences on the library cDNA. Within this bead-duplex mixture, Kamb also adds free identifier tag sequences that are labeled with a second label. Kamb states that the second label attached to the competing free oligonucleotide identifier tag sequences provides a means to control the amount of capture oligonucleotide and allows comparison between cellular transcripts that are weakly expressed and abundantly expressed.

The instant invention, in contrast, is directed to a method that includes providing an array composition comprising at least two subpopulations of microspheres, the microspheres of each subpopulation comprise a bioactive agent and at least two decoding attributes wherein at least one of the decoding attributes is an IBL that is different from the bioactive agent, and wherein the identifier binding ligand is directly attached to the microsphere. The bioactive agents are identified by detection of each of the first and second decoding attributes (claim 40). The detecting also includes detecting binding of a decoder binding ligand (DBL) to the IBL and detecting binding of a first target analyte to the bioactive agent on the first subpopulation of microspheres (claim 42).

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Anticipation of a claim requires that the reference teach every element of the claims. See M.P.E.P. § 2131. Thus, "a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." See *Verdegal Bros. v. Union Oil of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). It is imperative that the "identical invention be shown in complete detail as contained in the claim." See *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Kamb does not teach the "identical invention" as presently claimed. Kamb does not teach microspheres comprising a bioactive agent and at least a first and second decoding attribute wherein at least one of the decoding attributes is an identifier binding ligand that is different from the bioactive agent, and wherein the identifier binding ligand is directly attached to the microsphere.

In contrast, Kamb teaches that each bead has only one type of capture oligonucleotide attached to its surface, i.e. a bioactive agent as suggested by the Examiner (See Kamb at column 6, lines 4-5). Neither of the two labeled polynucleotides of Kamb are directly attached to the microsphere, as presently claimed.

Based on the foregoing, Kamb does not teach a method as claimed that includes providing an array comprising a population of microspheres comprising first and second subpopulations, wherein each of the microspheres comprises a bioactive agent and at least a first and second decoding attribute wherein at least one of the decoding attributes is an IBL that is different from the bioactive agent and wherein the IBL is directly attached to the microsphere. Because Kamb does not teach the identical invention as instantly claimed, Applicants submit the instant invention is novel in view of the cited reference.

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Because claims 41-and 43-49 depend directly or indirectly from claim 40 or 42 and incorporate all the limitations of claim 40, the above argument obviates the basis for this ground of rejection. Thus, claims 40-49 are not anticipated by Kamb.

Applicants respectfully request the Examiner to withdraw the rejection of the instant claims.

With respect to new claims 50 and 51, Applicants submit that these claims also are novel in light of Kamb. Claim 50 sets forth a method that includes providing an array composition comprising a population of microspheres comprising at least a first and a second subpopulation, wherein the microspheres of each subpopulation comprise a bioactive agent, and at least a first and a second decoding attribute wherein a first of the decoding attributes is an identifier binding ligand (IBL), wherein the IBL is different from the bioactive agent and the second decoding attribute comprises a physical attribute of the microsphere. The method further includes detecting each of the first and second decoding attributes to identify each of the bioactive agents.

In contrast, Kamb does not teach decoding attributes wherein one of the decoding attributes comprises an identifier binding ligand and one comprises a physical attribute of the microsphere. Again, while Kamb may disclose a microsphere with a bioactive agent as suggested by the Examiner, neither of the labeled polynucleotides of Kamb comprise a physical attribute of the microsphere as presently claimed. Accordingly, Applicants submit that claim 50 also is novel in light of Kamb.

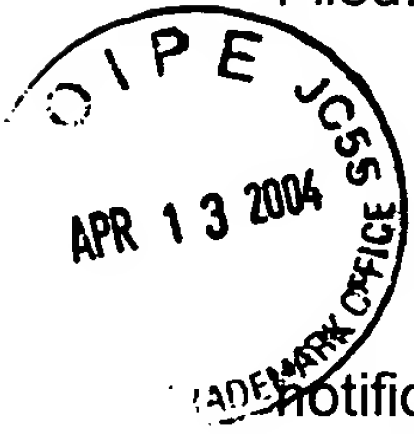
Claim 51 is directed to a method comprising providing an array composition comprising a population of microspheres comprising at least a first and a second subpopulation, wherein the microspheres of each subpopulation comprise a bioactive agent, and at least a first and a second decoding attribute wherein a first of the decoding attributes is an identifier binding ligand (IBL), wherein the IBL is different from the bioactive agent and the first and second decoding attributes are independent of

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each other. The method further includes detecting each of the first and second decoding attributes to identify each of the bioactive agents.

In contrast, the method disclosed in Kamb does not disclose the use of first and second decoding attributes, wherein the decoding attributes are independent of each other. Rather the decoding attributes in Kamb ultimately associate with the microsphere by binding either directly or indirectly with the bioactive agent. Thus, the labeled polynucleotides of Kamb are not independent of each other as presently claimed.

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### CONCLUSION

Applicants submit that the claims are in condition for allowance, and early notification to this effect is solicited. The Examiner is invited to contact the undersigned at (415) 781-1989 if any issues remain.

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